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MULTIPLE SCLEROSIS, WITH A REPORT OF TWO ADDITIONAL CASES, WITH NECROPSY.[1]

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Multiple sclerosis has been attracting much attention recently on account of the statements made regarding its infrequency in America. The views held regarding this subject are well presented in a paper by E. W. Taylor and J. W. Myer[2] published in 1903, and statistics are given by them. In contrast with these statements we find that L. Bruns[3] says that during a period of twelve years he had made the diagnosis of multiple sclerosis 70 times in 5,500 cases of nervous disease, or in 1 1-3 per cent. Twenty-one of these patients (30 per cent.) had symptoms of optic nerve disease. The diagnosis of multiple sclerosis was positive in only 38 of the 70 cases, and the 20 cases (above he speaks of 21 cases) with optic nerve affection were included in these 38 cases, making 58 per cent. Redlich,[4] in a paper published in 1903, remarks that multiple sclerosis is one of the most frequent diseases of the central nervous system.

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[1] Read before the Philadelphia Neurological Society, Dec. 22, 1903.

[2] Taylor and Myer. Boston Medical and Surgical Journal, April 9, 1903.

[3] Bruns and Stölting. Monatsschrift für Psychiatrie und Neurologie, Feb. and March, 1900.

Two cases of multiple sclerosis with necropsy were reported by one of us (Spiller[5]) in January, 1903, and two additional cases with necropsy have occurred in his services at the Polyclinic Hospital and the Philadelphia Hospital, and are reported in the present paper. These make six cases with necropsy reported in detail in America. The other two were reported by Burr and McCarthy[6] and by Hunt.[7] The frequency of multiple sclerosis in Europe is well known, and in 1898 attention was called by one of us (Spiller[8]) to the rarity of the diagnosis in America. At that time little or nothing had been said concerning this subject further than the remark in the edition of Dana's text-book published in 1892 and omitted in later editions.

The two additional cases with necropsy which we now report are as follows:

Case 1.—Miss M. C., twenty-eight years of age, a dressmaker by occupation, was referred to the Polyclinic Hospital, clinic of Dr. Spiller, August 19, 1903. The notes of the first examination made by Dr. Weisenburg are as follows:

Her father died from "consumption of the bowel." Her mother has rheumatism and is hysterical.

Miss C. began to menstruate when she was twelve years old, and has been very irregular. She began sewing when she was sixteen years of age. She has always been sickly and very nervous. Last September she noticed stiffness in her lower limbs when she got up in the morning, and she had difficulty in moving her lower limbs. She had also a numb sensation in these limbs and could not feel a pin prick at all. She never has had pain, although she has a sensation as of a tight band about the lower limbs. The sensation of stiffness has partially disappeared, but when she grows excited the paresthesia is increased. When she gets up in the morning she feels as though she were walking on rubber. She was confined to her bed for seven months. About last Christmas she noticed that she could not hold her urine so well as previously. She is obstinately constipated. Her memory is somewhat impaired, and the vision of the right eye seems diminished. The upper limbs have not been stiff. She says that at times she drags her left lower limb and may fall while walking.

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[4] Redlich. Die Deutsche Klinik, 1903.

[5] Spiller. American Journal of the Med. Sciences, Jan., 1903.

[6] Burr and McCarthy. Journal of Nervous and Mental Disease, 1900.

[7] Hunt. American Journal of the Medical Sciences, Dec., 1903.

[8] Spiller. The Philadelphia Polyclinic, 1898, p. 147.

She walks well with her eyes open, but is ataxic, although she does not fall, when her eyes are closed. She staggers when standing with eyes closed. The patellar reflex is exaggerated on each side, but more so on the left, and patellar clonus is obtained on the left side. Ankle clonus is not present. Babinski's sign is obtained on each side. The upper limbs are not affected. She has inframammary and inguinal tenderness.

The pupils are equal and the irides respond to light and in accommodation and convergence. The tongue is normal. The fifth and seventh nerves are not affected.

Miss C. was admitted to the Polyclinic Hospital September 9, 1903, and was seen by one of us (Dr. Spiller), and the notes then made are as follows:

The patient shows no muscular atrophy. The lower limbs are not spastic. The patellar reflex is a little exaggerated on each side, and there is a tendency to patellar clonus on each side, but no true patellar clonus. The Achilles jerk is normal on each side; Babinski's reflex is present on each side, the big toe being moved distinctly upward. Tactile sensation is preserved all over the body, but the patient says she feels a touch more distinctly in the upper limbs than in the lower. Pain sensation seems to be normal everywhere. She has some inguinal tenderness on the left side. The grasp of the hands is normal. Resistance to passive movement in the upper limbs is normal. The biceps tendon, triceps tendon and wrist reflexes are normal on each side. The pupils are equal, or possibly the right is a little smaller than the left. The reaction of the iris to light and in accommodation is normal. The tongue is protruded straight and shows no tremor and no atrophy. The facial muscles are not implicated on either side. Constipation is obstinate. Speech is not affected. Nystagmus was not observed in this or in any examination. Speech was not peculiar. A diagnosis of diffuse lesions in the posterior and lateral columns was made.

On September 16 a note was recorded that the patient was delirious and talked irrationally, and had had involuntary micturition while asleep. The patient was found excited and anxious about her condition, and probably worried by something that had occurred in her past history, but she was rational.

On September 18 she was sitting quietly in the ward. She got up suddenly and jumped out of a third story window. She was not unconscious as a result of this fall, and her head did not appear to be injured. Both bones of the right forearm were broken at the lower third and a compound comminuted fracture of the left wrist was found. The back of the trunk was badly contused over the buttocks as high as the lower thoracic vertebræ, and a depression over the spinal column was found at the lumbo-thoracic junction. The lower limbs were paralyzed.

On September 19 the following notes were made: The patient talks freely and it is evident that she is worried by some private affair. The bowels and bladder are paralyzed. She has complete paralysis of the lower limbs and cannot even move the toes. The patellar reflex is lost on each side. There is no ankle clonus and Babinski's sign is not obtained. The level at which sensation for touch is preserved can not be accurately determined because of the patient's inability to fix her attention on the examination. A pin prick is not felt at all in the left lower limb, and very imperfectly in the right lower limb; but is felt over the whole of the abdomen. The head and upper limbs except where the fracture has occurred, are not affected.

An X-ray examination made September 22 seemed to show an injury of the second and third lumbar vertebræ.

The patient had fever about 101°, varying from 1½ to 2° daily, pulse 116 to 132, respiration 24 to 28. She became gradually weaker and died October 3.

The necropsy was made by Dr. Randolph. His notes abbreviated are as follows: Extravasation of blood is found over the lower anterior surface of the sternum, and especially over the anterior surface of the spinal column. A subdural hemorrhage is present over both occipital lobes, but the skull is not fractured. The first lumbar vertebra is fractured, and the body of this vertebra is displaced backward. At the seat of fracture the spinal cord is softened and disorganized, but above this level the cord appears to be normal.

The microscopical examination gives the following results:

The spinal cord below the third lumbar segment is softened as a result of the fracture of the first lumbar vertebra. Sections from the lower part of the second lumbar segment or upper part of the third lumbar segment show several areas of sclerosis, and the area of the left crossed pyramidal tract contains fewer nerve fibers than in normal sections, and presents the appearance of secondary degeneration. Symmetrical areas of sclerosis are found in the anterior and posterior columns. In sections stained by hemalum and acid fuchsine a slight round cell infiltration is seen about some of the vessels in the spinal cord and in some parts of the pia. The nerve cells of the anterior horns stained by the acid fuchsine are much degenerated. They are swollen and their nuclei are eccentric. This alteration is probably the result of the fracture. The Nissl method could not be employed. Sections from about the same level stained by the Marchi method show much recent degeneration widely distributed. Numerous bundles of degenerated fibers coming from the posterior

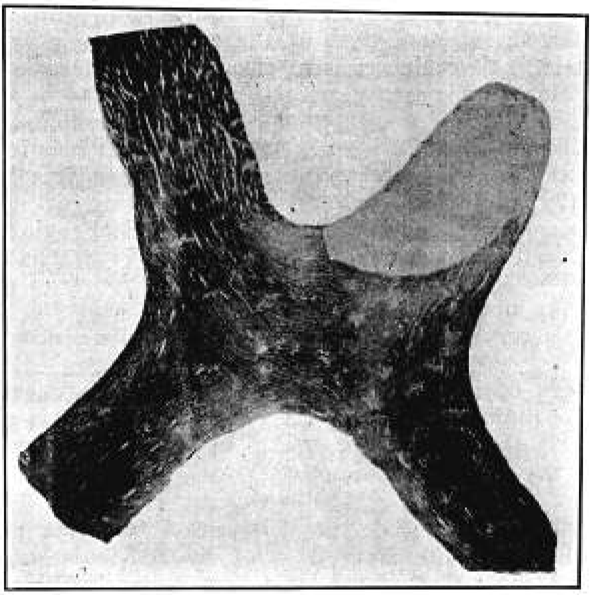

Fig. 1. Photograph of the optic chiasm and optic nerves from Case 1, showing the right optic nerve sclerotic as high as the chiasm and sharply defined from the normal tissue of the chiasm. The left optic nerve is well stained.

roots are seen entering the left posterior horn. Similar bundles are not found in the right posterior horn, because at this level the right posterior horn was implicated in a sclerotic area and the medullary sheaths of many of the nerve fibers coming from the posterior roots have disappeared.

At the tenth thoracic segment the areas of sclerosis are numerous. Marchi sections from this level show much recent degeneration in the sclerotic areas, as well as some degeneration that is secondary and resulting from the fracture of the spinal column.

The areas of sclerosis are even more numerous at the eighth thoracic segment than at the tenth thoracic segment. At the seventh thoracic segment the areas of sclerosis in the anterior columns are symmetrical.

Throughout the thoracic region some round cell infiltration is found about the blood vessels of the cord, but it is impossible to determine any direct connection between this infiltration and the sclerotic areas.

Sclerotic areas are found in the lower cervical region. The nerve cells of the anterior horns at this level are not much altered. The upper part of the cervical region was not obtained at the necropsy.

Sclerotic areas are not seen in the medulla oblongata or pons.

The right optic nerve is almost completely degenerated as far as the commissure, where the degenerated area is sharply marked off from the normal area. The left optic nerve is not degenerated.

Case 2.—P. B., a male, aged twenty-four years, came to the Polyclinic Hospital May 19, 1898, to the service of one of us (Dr. Spiller). He had been a collector, and in this occupation had walked much and been much exposed to wet and cold; later he had worked in a machine shop.

The family history is unimportant. The patient denies venereal disease but says he had masturbated freely. He has been losing power in his lower limbs for the past nine months, but has no loss of power in the upper limbs, and no pain anywhere, no headache and no involuntary seminal emissions. About five months previously he had difficulty in holding his urine, but only during a period of about two weeks. He has been constipated during the past two months. He has no girdle sensation. Sight has been poor during the past year. Six or seven months previously he frequently stubbed his toes in walking.

His gait is very ataxic. Romberg's sign is present. The patellar reflex is much exaggerated on each side, but ankle clonus is not obtained on either side. Achilles jerk is very prompt on each side. Sensation is normal everywhere. The upper limbs are distinctly ataxic. The irides react promptly to light and in accommodation, and the voluntary movements of the eyeballs is good. Slight nystagmus is present when the patient looks to the right and upward. Contraction of both visual fields is present, and is most marked in the temporal side. There are no gross changes in the eyegrounds. The patient was lost sight of after he had been coming to the clinic for a long time, but in the early part of 1901 he was admitted to the Philadelphia Hospital and soon came into the service of Dr. Spiller. He had been confined to his bed about a year on account of weakness of the lower limbs. Atrophy had not developed.

Notes made April 9, 1901, are as follows: The patient is unable to walk at all. He can stand a few minutes with support, but his legs soon give away. Both upper and lower limbs are incoördinate, and the left lower limb more so than the right. The reaction of the iris to light and in accommodation is slow. Nystagmus is present. The extraocular muscles are not affected. Beginning optic atrophy is found in each eye. The facial muscles are not implicated, and the tongue is protruded straight.

September 10,1901.—The lower limbs are somewhat emaciated, but not excessively so. No contractures are observed anywhere. The lower limbs are spastic, and the spasticity is increased by passive movements. The patellar reflexes and the Achilles tendon reflexes are exaggerated, and ankle clonus is obtained. Sensation for touch and temperature is diminished in the lower limbs, but for pin prick is normal. Babinski's sign is present on each side. Both lower limbs are paralyzed, but the toes can be moved slightly. He is unable to raise himself in bed, and turns his body over with great difficulty. The voluntary movements of the upper limbs are good. Speech is weak and slow, but not scanning and not explosive.

July 31, 1903.—There is slight ptosis of each upper eyelid. Nystagmus is present when the patient looks directly in front of him. Speech is somewhat explosive but not scanning. The upper limbs are weak. The man is emaciated. Intention tremor is present and more marked in the left upper limb than in the right. Tactile sensation is lost in the portion of the body between the knees and a line two inches below the nipples, but sensation for pin prick is preserved everywhere. He has no incontinence of urine and feces.

An examination of the eyes made about this time showed that the temporal side of the disc in each eye was abnormally white, suggesting incipient atrophy.

The man died August 10, 1903, from phthisis and chronic nephritis.

A microscopical study of the spinal cord and brain from this case gives the following results:

The areas of sclerosis are very extensive throughout the spinal cord and medulla oblongata.

Sclerotic areas are found in the sacral region, and those in the posterior columns on both sides of the cord are symmetrical.

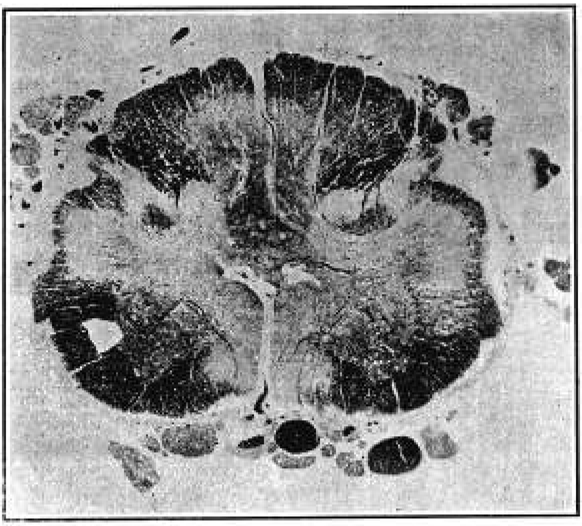

Fig. 2. Photograph of a section of the lumbar cord from Case 2, showing remarkable symmetry of the sclerotic areas in the anterior, lateral and posterior columns.

In the mid lumbar region the areas of sclerosis are remarkably symmetrical in the anterior, lateral and posterior columns. The areas in the lower, middle and upper thoracic regions are symmetrical.

The sclerosis in this case is somewhat different from that in many cases of multiple sclerosis, in that many of the degenerated areas are not sharply defined from the normal tissue, but shade off into it.

In the middle of the cervical swelling the sclerotic areas on the two sides of the cord are still nearly symmetrical.

Sclerotic areas are numerous in the medulla oblongata, and they are found also in the pons, cerebral peduncles, cerebral cortex and optic chiasm. Both the right and left optic nerves are almost completely degenerated except in certain parts of the periphery of each nerve.

The Marchi stain shows recent degeneration along the edges of some of the sclerotic areas. Perivascular round-cell infiltration in moderate intensity is found in the pia and within the spinal cord, but is pronounced in the pia of the optic chiasm and within the chiasm.

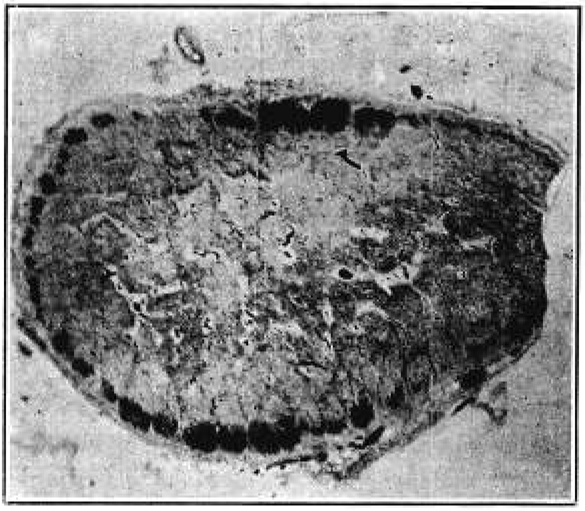

Fig. 3. Photograph of one of the optic nerves in Case 2, showing a sclerotic area implicating the transverse section of the nerve except at the periphery.

The nerve cells of the anterior horns in the lumbar and cervical regions stain well by the Nissl method. A brief abstract of each case is as follows:

Case 1.—The patient, a woman twenty-eight years old, had always been sickly and nervous. She noticed stiffness and weakness of the lower limbs in September, 1902. She complained of paresthesia in these limbs and had some disturbance of objective sensation. About Christmas, of 1902, she had difficulty in holding the urine. Vision of the right eye appeared to be diminished. The gait was not striking when the eyes were open, but was ataxic when the eyes were closed. The patellar reflex was a little exaggerated on each side. Babinski's sign was present on each side. The upper limbs and head were not affected. Speech was not peculiar and nystagmus was not observed. The woman while in the hospital jumped from a third story window and died after an injury received from the fall. She had a fracture of the first lumbar vertebra. Areas of sclerosis were found throughout the spinal cord, and the right optic nerve appeared almost completely degenerated.

Case 2.—This patient first came under the observation of one of us (Dr. Spiller) in 1898, and had been under his care much of the time since until the patient's death. In 1898 the man was twenty-four years old. He had been exposed to wet and cold. The notes made in 1898 state that he had been losing power in his lower limbs for nine months, but had no loss of power in the upper limbs and no pain anywhere. He had had difficulty in holding the urine during a period of about two weeks. Sight was poor. Gait was ataxic. Romberg's sign was present. The patellar reflex was much exaggerated. Sensation was normal everywhere. The upper limbs were ataxic. Slight nystagmus was present.

In 1901 he was unable to walk at all. Beginning optic atrophy was found in each eye. Speech was slow but not scanning.

In July, 1903, intention tremor was observed in the upper limbs. He had incontinence of urine and feces. Tactile sensation was much impaired in the lower limbs and trunk. The temporal side of the disc in each eye was abnormally white, suggesting incipient atrophy.

Sclerotic areas were found throughout the cord, medulla oblongata, pons, cerebral peduncles, and in the white matter and cortex of the cerebrum. The areas in the spinal cord were remarkably symmetrical.

Flatau and Koelichen[9] say that the number of published cases in which multiple sclerosis caused the clinical appearance of transverse myelitis is not great. They refer to the cases of Pitres, Siemerling, and Nonne, and report a case in which the symptoms were flaccid paralysis of the lower limbs, incontinence of urine and feces, and decubitus; sensation was not disturbed. The upper limbs and cranial nerves were not implicated, and the patient did not have intention tremor, nystagmus, scanning speech or mental symptoms. An ophthalmoscopic examination was not made.

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[9] Flatau and Koelichen. Deutsche Zeitschrift für Nervenheilkunde, Vol. 22, Nos. 3 and 4, p. 250.

The first case that we report in this paper was suggestive of transverse myelitis, but it was supposed to be a case in which diffuse lesions were present in the lateral and posterior columns, and certain facts in the history suggested syphilis. The fall from a third story window during the time the case was being carefully studied caused symptoms that masked those originally present. An examination of the eyegrounds would probably have shown alteration of the right optic disc, and this examination would doubtless have been made if the accident referred to had not occurred soon after the patient entered the hospital.

The frequent implication of the optic nerves in multiple sclerosis was known to Charcot some thirty years ago. It has been mentioned repeatedly by Oppenheim, and more recently the subject has received attention from Bruns and Stölting and others. A person with sclerotic patches in the optic nerve may have little or no disturbance of vision, and the ophthalmoscopic examination may reveal an unsuspected condition, especially as the disease of the optic nerve may be among the first or even the first sign of the multiple sclerosis. Sclerotic patches may occur in any part of the visual tracts as far back as the cortex of the occipital lobe. According to Bruns and Stölting the chiasm is frequently the seat of sclerotic areas. The ophthalmoscopic change consists often of pallor of the temporal side of the disc; optic neuritis or optic atrophy also may be found.

In both the cases reported in this paper optic nerve degeneration was pronounced, and it was present also in the other two cases reported by one of us (Spiller), and also in the case of Burr and McCarthy. An examination of the eyegrounds is therefore of great importance in every case presenting symptoms that could be attributed to multiple sclerosis, because the disturbance of vision, as in both the cases reported in this paper may be slight as compared with the alteration of the optic nerves.

Bruns and Stölting[10] confirm the observations of Oppenheim regarding disturbances of the bladder and of sensation, at least in the later stages of the disease. Vesical symptoms and sensory disturbances were present in both of our cases.

The degeneration of the posterior root fibers of the mid lumbar segment on the left side in the first case was caused by the fracture of the first lumbar vertebræ and injury to the spinal roots. The degeneration of the medullary sheaths by the Marchi method was very distinct, and the degenerated fibers could be seen entering the posterior horn of the left side in large numbers. As the posterior roots within the cord on the right side at the same level were implicated in a sclerotic area, and the medullary substance of these fibers had disappeared, no degeneration of these roots by the Marchi method could be detected. This observation shows that the patellar reflex may be exaggerated, even though the medullary sheaths about the fibers concerned in the reflex have disappeared. It has been known that the function of nerve fibers within the spinal cord may be preserved after the medullary sheaths of these fibers have disappeared, and our case shows that the same is true of the fibers concerned in the tendon reflexes.

Flatau and Koelichen discuss the pathological findings of multiple sclerosis, whether they are inflammatory or not, and they make the statement that most of the recent investigators favor the inflammatory theory. They refer to Ribbert, Cramer, Bikeles, Goldscheider, Balint, and others. Redlich, however, does not accept the inflammatory theory. Flatau and Koelichen, from a study of their case of multiple sclerosis and from their investigations of the literature, conclude that multiple sclerosis should be classed with disseminated myelitis. Strümpell, in a note at the end of their paper, makes the criticism that it would be better to regard their case as one of acute disseminated myelitis, instead of multiple sclerosis, and he insists on making a sharp distinction between the two diseases.

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[10] Bruns and Stölting. Monatsschrift für Psychiatrie und Neurologie, Feb. and March, 1900.

It is exceedingly difficult to determine the relation of multiple sclerosis to multiple myelitis. In the latter disease we do not find usually the areas of sclerosis sharply defined, at least to the naked eye, from the surrounding normal tissue. In our second case many areas of sclerosis shade off into the normal tissue, and at some places perivascular cellular infiltration is found, and yet this is unquestionably a typical case of multiple sclerosis. In our first case the perivascular cellular infiltration is distinct at certain places but it is impossible to establish a close relation between these and the sclerotic areas. This should be a suitable case for this purpose, as death occurred less than a year after the first definite symptoms of multiple sclerosis were manifest, and from a cause independent of this disease.

Redlich has called attention to the symmetry sometimes found in the areas of the two sides of the cord in multiple sclerosis. The symmetry throughout the spinal cord in our second case is extraordinary, and suggests a vascular origin or a defect in the development of the cord. We have never seen in any case of multiple sclerosis such symmetry extending throughout the cord, and yet we have at our command sections from many cases of multiple sclerosis. Fig. 3 shows the symmetrical areas on the two sides of the cord in the lumbar region.